Answer 1:

Bibliographic Information

Induction of apoptosis in metastatic foci from human gastric cancer xenografts in nude mice and reduction of circulating tumor cells in blood by 5-FU and 1-hexylcarbamoyl-5-fluorouracil. Nakanishi, Hayao; Abe, Atsushi; Inada, Kenichi; Tsukamoto, Tetsuya; Yasui, Kenzo; Tatematsu, Masae. Laboratory Pathology, Research Institute, Aichi Cancer Center, Nagoya, Japan. Journal of Cancer Research and Clinical Oncology (1999), 125(12), 660-668. Publisher: Springer-Verlag, CODEN: JCROD7 ISSN: 0171-5216. Journal written in English. CAN 132:198 AN 1999:759921 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Antimetastatic effects of 5-FU and its deriv., 1-hexylcarbamoyl-5-fluorouracil (HCFU) on human gastric cancer micrometastasis and their mode of action were evaluated, using a spontaneous lung metastasis model (HY-1) in nude mice. Metastases were 1st detected in the lung from 4 wk after s.c. transplantation, growing intravascularly and forming micrometastases at 100% incidence by 6 wk after implantation. Lung metastasis in mice bearing s.c. tumors was inhibited by HCFU at doses of 100-150 mg kg-1 day-1 without severe toxic side-effects, when orally administered 3 times per wk either from week 4 or week 6 to 9 wk after implantation. Spontaneous lung metastasis was also inhibited by the administration of 5-FU, but to lesser extent than with HCFU at equimolar low doses. Apoptosis within primary tumors and lung metastatic foci, as detected by the terminal-deoxynucleotidyltransferase-mediated dUTP nick-end labeling method, was found to be enhanced by HCFU as well as 5-FU administration at doses of >100 mg kg-1 day-1 and 50 mg kg-1 day-1 resp. However, proliferating activity of the metastatic foci, as evaluated by MIB-1 immunostaining, was not suppressed by HCFU or 5-1 V treatment. Furthermore, polymerase chain reaction anal. using human specific primers for the β-globin gene, which proved to be capable of detecting 10 tumor cells/mL mouse blood, revealed that circulating tumor cells in the peripheral blood of mice bearing primary tumors were reduced by HCFU or 5-FU administration. These results indicate that circulating tumor cells in blood and micrometastases in the lung are sensitive to these chemotherapeutic agents, and suggest that the anti-metastatic effect of these agents is mediated, at least in part, by enhanced apoptosis rather than by inhibition of cell proliferation.

Answer 2:

Bibliographic Information

Modulation by l-leucovorin of 1-hexylcarbamoyl-5-fluorouracil antitumor activity on human gastric and colon carcinomas serially transplanted into nude mice. Kubota, Tetsuro; Kase, Suguru; Furukawa, Toshiharu; Tanino, Hirokazu; Kuo, Tsong Hong; Saikawa, Yoshiro; Nishibori, Hideki; Ishibiki, Kyuya; Kitajima, Masaki; et al. Sch. Med., Keio Univ., Tokyo, Japan. Anticancer Research (1992), 12(5), 1549-53. CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 118:52020 AN 1993:52020 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Exptl. biochem. modulation of 1-hexylcarbamoyl-5-fluorouracil (HCFU) with l-leucovorin (LV) was carried out using human gastric (H-111) and colon (Co-4) carcinoma xenografts serially transplanted into nude mice. Thirty-five or 70 mg/kg HCFU dissolved in 0.2 mL of 1% hydroxymethyl cellulose was administered orally daily for 3 wk except Sundays, and 50, 100, 200 or 300 mg/kg LV dissolved in 0.2 mL physiol. saline was administered po 30 min before administration of HCFU. The biochem. modulated antitumor activity was evaluated in terms of actual tumor wt., the relative mean tumor wt. and the degree of inhibition of thymidylate synthetase (TS) in the tumors at the end of the expts. Although 35 mg/kg HCFU was ineffective against gastric carcinoma H-111, combination with 200 or 300 mg/kg LV resulted in a pos. antitumor effect of HCFU on this strain without any increase of side effects in terms of body wt. loss and mouse mortality. The colon carcinoma strain Co-4 showed marginal sensitivity to HCFU (35 mg/kg) alone, but 50 or 100 mg/kg LV modulated the antitumor activity of HCFU on Co-4 to produce a significant pos. effect without any increase in toxicity, and HCFU administered with 100 mg/kg LV was more effective than the max. tolerated dose of HCFU (70 mg/kg) alone. The TS inhibition rate was closely related to the biochem. modulation of HCFU antitumor activity by LV, suggesting that the modulation involves an increase of the ternary complex of TS, 5,10-methylene tetrahydrofolate from LV and 5-fluorodeoxyuridine 5'-monophosphate (FdUMP). Combination of HCFU and LV is therefore thought to be useful in increasing the antitumor activity of

HCFU on gastrointestinal carcinomas without enhancing its toxicity.

Answer 3:

Bibliographic Information

In vivo inhibitory effect of anticancer agents on human pancreatic cancer xenografts transplanted in nude mice. Imai, Shiro; Nio, Yoshinori; Shiraishi, Takahiro; Manabe, Tadao; Tobe, Takayoshi. Fac. Med., Kyoto Univ., Kyoto, Japan. Anticancer Research (1991), 11(2), 657-64. CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 115:174179 AN 1991:574179 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Pancreatic cancer is one of the neoplasms resistant to chemotherapy. In the present study human pancreatic cancer xenografts (3 adenocarcinomas and 1 cystoadenocarcinoma) were s.c. transplanted in nude mice and after the tumors grew to 100-300 mm3, the mice were i.p. administered with mitomycin C (MMC), adriamycin (ADR), 5-fluorouracil (5-FU), carboquone (CQ), cisplatinum (CDDP), nimustine chloride (ACNU) or DWA2114R at 1/3 LD50 on days 0, 4, and 8. The tumor sizes on day 12 were compared with those on day 0. MMC and CQ significantly inhibited the tumor growth of 3 lines, and ACNU, CDDP and ADR inhibited the growth of 1 line. Further, 5-FU, futrafur, carmofur, UFT, and L-phenylalanine mustard (L-PAM) were orally administered to mice into which 1 adenocarcinoma line had been transplanted. While none of fluoropyrimidines inhibited tumor growth, L-PAM at 4 mg/kg significantly inhibited growth, although it was accompanied by severe body wt. loss. In the present study several agents significantly inhibited tumor growth, but none of them could induce the regression of the tumor when used singly. These results suggest that CQ, ACNU, CDDP and L-PAM may be applied to the chemotherapy of pancreatic cancer. However, the effect of a single agent is restricted and the development of new combination treatments is urgently required.

Answer 4:

Bibliographic Information

Combined effects of interferon α-A/D with fluoropyrimidine derivatives in subrenal capsule assay. Nishiyama, Masahiko; Takagami, Shinichi; Kirihara, Yoshimasa; Saeki, Toshiaki; Niimi, Ken; Kim, Ryungsa; Jinushi, Kazuto; Toge, Tetsuya; Niimoto, Minoru; Hattori, Takao. Res. Inst. Nucl. Med. Biol., Hiroshima Univ., Hiroshima, Japan. Gan to Kagaku Ryoho (1988), 15(8), 2285-90. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 109:204561 AN 1988:604561 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Synergistic, additive, or subadditive antitumor effects were obsd. following the combined administration of interferon α-A/D with fluoropyrimidine derivs. (i.e., 5-FU, tegafur, and 5'-deoxy-5-fluorouridine, UFT, and 1-hexylcarbamoyl-5-fluorouracil) to athymic mice bearing human tumor xenografts (H-111 and SH-10 gastric cancers and CH-5 colon cancer). The combinations were not effective against CH-4 colon cancer of human.

Answer 5:

Bibliographic Information

Subrenal capsule assay using nude mice as a predictor of the response of the gastric cancer to chemotherapy. Yamauchi M; Satta T; Ito A; Kondo K; Akiyama S; Ito K; Watanabe T; Takagi H Department of Surgery II, Nagoya University School of Medicine, Japan Journal of surgical oncology (1991), 47(2), 98-101. Journal code: 0222643. ISSN:0022-4790. Journal; Article; (JOURNAL ARTICLE) written in English. PubMed ID 1905767 AN 91287313 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Feasibility of utilizing human gastric cancers as first transplant generation xenografts in nude mice for determining tumor sensitivity to chemotherapeutic agents was demonstrated by applying subrenal capsule (SRC) assay. A total of 55 human gastric tumors from patients were tested in this assay. Mitomycin-C (MMC) and hexycarbamyl-5-FU (HCFU, 5-FU derivative) were selected for the treatment of these patients after surgery and also for this assay as first transplant. Evaluable rate of MMC in this assay was 92.7% and that of HCFU was 90.9%. Sensitivity of tumors to MMC was 25% and to HCFU was 32%. Correlation between response to chemotherapy of human tumors in patients and in nude mice was 78.6%. These results indicate that this assay could predict effective drugs for patients with gastric cancer.

Answer 6:

Bibliographic Information

Effect of concomitant use of anticancer drugs and a Ca2+ antagonist, on human gastric cancer transplanted into nude mice. Nakatani K; Watanabe A; Nishiwada T; Sawada H; Okumura T; Yamada Y; Yano T; Shino Y; Nakano H 1st Department of Surgery, Nara Medical University Nippon Gan Chiryo Gakkai shi (1990), 25(1), 98-102. Journal code: 7505713. ISSN:0021-4671. (ENGLISH ABSTRACT); Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in Japanese. PubMed ID 2324591 AN 90217757 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

We examined the effect of concomitant use of anticancer drugs such as Carmofur or 5-FU and Nicardipine, a Ca2+ antagonist, on human gastric cancer transplanted into nude mice, and obtained the following results: 1. Combined administration of Carmofur or 5-FU together with Nicardipine caused potentiation of an antitumor effect. 2. After Carmofur was used together with Nicardipine, the FU level in the tumor tissue was significantly elevated. In conclusion, it was found that in the combined use of Carmofur or 5-FU together with Nicardipine, a Ca2+ antagonist, caused a higher level of the FU in tumor tissue and potentiation of an antitumor effect on human gastric cancer transplanted into nude mice.

Answer 7:

Bibliographic Information

Antitumor effects of 5-fluorouracil-bound organic silicon compound. Fukushima K Division of Chemotherapy, School of Medicine, Keio University Gan to kagaku ryoho. Cancer & chemotherapy (1989), 16(9), 3243-50. Journal code: 7810034. ISSN:0385-0684. (ENGLISH ABSTRACT); Journal; Article; (JOURNAL ARTICLE) written in Japanese. PubMed ID 2782916 AN 89391543 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

5-fluoro-3,4-dihydro-2,4-dioxo-N-[2-2- (dimethylphenylsilyl)ethylthioethyl]-1(2H)-pyrimidinocarb oxamide (SDK-12B-5), a novel antitumor agent, is covalently linked with 5-fluorouracil (5-FU) and 2-[(2-dimethylphenylsilyl)ethylthio] ethylamine(SDK-103) which possesses itself antitumor activity against murine solid tumors. It has a broad antitumor spectrum in experimental tumor systems including murine leukemias. Furthermore, SDK-12B-5 administered p.o. with various treatment schedules inhibited significantly the tumor growth of human breast cancer (MX-1), colon cancer (Co-4) and lung cancer (LX-1 and OAT) cells in BALB/c nu/nu mice and the chemotherapeutic index was about 10 for 4 different human cancer xenografts. In the Lewis lung carcinoma (LLC) metastasis model, SDK-12B-5 in combination with amputation of tumors inhibited significantly both the lymph node metastases and lung metastases of LLC and prolonged the life span (%ILS:91%) of BDF1 mice. We also found that the cell killing effect of SDK-12B-5 was affected by both

concentration and exposure time in cultured human lung cancer (OAT) cells using soft-agar colony assay. A significant augmentation of delayed type hypersensitivity (DTH) response induced by SDK-12B-5 in comparison with the mixture of SDK-103 and 5-FU was seen when it was administered p.o. simultaneously with the immunization of sheep red blood cell (SRBC) in retired CD1 mice. From the studies on tissue distribution and pharmaco-kinetics of SDK-12B-5 by HPLC and ICP analysis. the persistence of SDK-12B-5 levels in serum and tumors was correlated with the findings that a maximum chemotherapeutic effect was obtained when SDK-12B-5 was administered p.o. repeatedly with every other day to avoid the cumulative toxicity.

Answer 8:

Bibliographic Information

The antiproliferative effects of fluoropyrimidine derivatives against human tumor xenografts in a subrenal capsule assay. Nishiyama M; Takagami S; Kirihara Y; Saeki T; Hirabayashi N; Nosoh Y; Niimoto M; Hattori T Department of Surgery, Hiroshima University, Japan The Japanese journal of surgery (1988), 18(6), 725-8. Journal code: 1302176. ISSN:0047-1909. (COMPARATIVE STUDY); Journal; Article; (JOURNAL ARTICLE) written in English. PubMed ID 2977626 AN 89236816 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

The antiproliferative effects of the fluoropyrimidine derivatives, 5-fluorouracil (5-FU), 1-(2-tetrahydrofuryl)-5-fluorouracil (Tegafur), UFT, 1-hexylcarbamoyl-5-fluorouracil (HCFU), and 5'-deoxy-5-fluorouracil (5'DFUR), were investigated in a 4 day subrenal capsule assay. The antiproliferative effects against two human tumor xenografts established in athymic mice were examined after treatment with three different doses of each anticancer agent, and the adequate dose of each anticancer agent in this experimental system was estimated as: 473 mg/kg for Tegafur, 433 mg/kg for UFT, 50 mg/kg for HCFU and 185 mg/kg for 5'DFUR, respectively. A comparative study of the antiproliferative effects of fluoropyrimidine derivatives was carried out against 7 xenografts. According to our criteria of positive tumor response, the effective rates were: 1 of 7 (14.3 per cent) by 5-FU, 2 of 7 (28.6 per cent) by Tegafur, 2 of 7 (28.6 per cent) by UFT, 1 of 6 (16.7 per cent) by HCFU, and 1 of 4 (25.0 per cent) by 5'DFUR, respectively. Although no statistical differences were demonstrated between the agents, the utility of a chemosensitivity test before clinical use was suggested.

Answer 9:

Bibliographic Information

Inhibition of thymidylate synthetase and antiproliferative effect by 1-hexylcarbamoyl-5-fluorouracil. Nishiyama M; Takagami S; Kim R; Kirihara Y; Saeki T; Jinushi K; Niimoto M; Hattori T Dept. of Surgery, Research Institute for Nuclear Medicine and Biology, Hiroshima University Gan to kagaku ryoho. Cancer & chemotherapy (1988), 15(11), 3109-13. Journal code: 7810034. ISSN:0385-0684. (ENGLISH ABSTRACT); Journal; Article; (JOURNAL ARTICLE) written in Japanese. PubMed ID 3190249 AN 89049202 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

In order to estimate tumor chemosensitivity of fluoropyrimidine derivative, inhibition of thymidylate synthetase (TS) was investigated using a nude mouse experimental system. Four human tumors xenografted in nude mice; H-111, SH-8 and SH-10, each established from gastric cancer, and EH-1 from esophageal cancer, were used. When the transplanted tumor volumes reached to approximately 200 mm3, 1-hexylcarbamoyl-5-fluorouracil (HCFU) was given for 5 days. Tumors was removed for the measurement of total and free TS at 0 hr, 6 hrs and 24 hrs after the last administrations. Simultaneously, the anti-proliferative effects were investigated according to the therapeutic protocol of NCI. No positive correlation between the inhibition rate of TS and the anti-proliferative effects was observed, although the absolute values of free TS were similar to the tumor inhibition rates. The measurement of total TS provided a highest concentration in

SH-8, while extremely low in EH-1. On the analysis of free TS, a significant increase of the concentration was observed at 24 hrs after the last administration compared with at 6 hrs in SH-8. These results indicate that free TS had a potentiality as a new parameter for predicting tumor chemosensitivity of fluoropyrimidine derivative and the analysis of TS should be affected strongly by the characteristics of enzymic activity of examined tumor.

Answer 10:

Bibliographic Information

Effect of post operative maintenance chemotherapy against ovarian cancer. Sawada M; Ozaki M; Hongo J; Hirota Y; Inagaki M Nippon Sanka Fujinka Gakkai zasshi (1987), 39(7), 1115-20. Journal code: 7505749. ISSN:0300-9165. (ENGLISH ABSTRACT); Journal; Article; (JOURNAL ARTICLE) written in Japanese. PubMed ID 3611882 AN 87281917 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

The significance of maintenance chemotherapy after surgery for ovarian cancer was examined using a human tumor-nude mouse system. Experiment 1: The human yolk sac tumor of the ovary (YST-2) heterotransplanted into nude mice was used. The tumor-bearing mice were administered 100 mg/kg of 1-Hexylcarbamoyl-5-fluorouracil (HCFU) orally for 60 days after tumor resection. Control mice were given 0.1 ml 0.3% methylcellulose after tumor resection. When the tumor was completely resected by surgery, HCFU treatment succeeded in decreasing the recurrence rate of the tumor, and in improving the survival rate of the host mice. However, when the macroscopic tumor was left in the host mouse, HCFU treatment did not affect either the recurrence rate of the tumor or the survival rate. Experiment 2: The human poorly differentiated adenocarcinoma of the ovary (OVA-2) heterotransplanted into nude mice was used. Administration of 100 mg/kg of HCFU immediately after the heterotransplantation into nude mice for 60 days suppressed the tumor growth. HCFU treatment improved the survival rate of the tumor-bearing mice. The antitumor effect of HCFU on the OVA-2 tumor was confirmed by histological examination. These experiments revealed that the maintenance chemotherapy after surgery for ovarian cancer was important in the effective treatment of the patient (tumor-bearing host).

Answer 11:

Bibliographic Information

Experimental chemotherapy of ovarian cancers heterotransplanted in nude mice. Sawada M Nippon Sanka Fujinka Gakkai zasshi (1985), 37(8), 1400-8. Journal code: 7505749. ISSN:0300-9165. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in Japanese. PubMed ID 2995515 AN 86009866 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))